Trihexyphenidyl (Artane) Intoxication due to Overdosage with Suicidal Intent

G. F. MORGENSTERN, M.D.,* *Verdun, Que.*

THROUGH the aftercare clinic of Verdun Protestant Hospital, Verdun, Que., many patients are followed up to whom phenothiazines are administered on an outpatient basis. A number of these patients require antiparkinsonian drugs to control the side effects of their phenothiazine medication. When they are provided with a few weeks' supply of such drugs to take to their homes, these patients have at hand enough medication to cause serious intoxication if large amounts are taken at once.

This was the experience of F.N., a 29-year-old chronic hebephrenic schizophrenic male patient who had been in and out of the hospital four times since his first admission at the age of 17 years. He had responded well to the administration of 200 mg. chlorpromazine (Largactil) and 2 mg. trihexyphenidyl (Artane), each thrice daily, and was discharged on a trial basis to the after-care clinic, on this schedule as maintenance dosage. In the weeks prior to readmission, his family noted a return of his familiar symptoms of irritability, restless pacing, preoccupation and nocturnal laughing, and concluded that he was neglecting his medications. When he admitted this and they tried to convince him to take them, he was stubbornly negativistic. One evening while alone at home, he impulsively swallowed an entire supply of 90 tablets of Artane which had been given to him at the clinic; each tablet contained 2 mg. trihexyphenidyl.

Over the next two days his family noted that he manifested a progressive onset of drowsiness and had a warm, flushed skin. When he became difficult to rouse and a rash appeared, his parents brought him to hospital. His symptoms presented a difficult diagnostic problem in the absence of an adequate history. It was not until the third day after his admission that the patient was sufficiently responsive to confirm the suspicion that he had consumed an overdose of his medication.

On admission, the patient was stuporous, responding only to simple commands. He was irritable, waking with a start when roused and resisting any manipulation or change of position from that of generalized partial flexion which he maintained. At times he muttered to himself, shifted restlessly in his bed, and occasionally picked at the bedclothes or plucked hallucinatory objects out of the air.

He was febrile, with a temperature of 101° F., and had respirations somewhat deeper than normal at a rate of 24/sec. His pulse was regular at 92/min., and his blood pressure was 110/70 mm. Hg. His pulse and blood pressure during his previous admission had been 80/min. and 130/70 mm. Hg, respectively.

His skin was strikingly dry and flushed. Shallow, irregular, round blebs, up to one inch across and filled with opalescent straw-coloured fluid, were observed on the shoulders, hip, knees and feet, in no particular pattern. These blebs were surrounded by a 3-mm. halo of erythema.

The conjunctivae were moderately injected; the pupils were 8 mm. in diameter and feebly responsive to light. Extraocular movements of normal scope could be obtained by turning his head while the eyes were fixed on a source of light, but convergence was not demonstrated. Examination of the optic fundi revealed no abnormalities.

The mucosa of the nose and mouth was dry, and a sticky mucous exudate was swallowed as it was coughed up. The chest was clear on percussion and auscultation, and heart sounds were normal. Palpation of the abdomen met with generalized resistance and evasive movements. The patient was incontinent of urine several times daily in small amounts. The bladder was not palpably distended.

Neurological examination, besides the aforementioned signs, showed generalized hypotonia, with weakly present tendon reflexes, absent abdominal and cremasteric reflexes, and extensor plantar responses. He was too weak to sit without support.

During the next three days, his temperature rose to 103° F., then returned to normal. He remained delirious, becoming more restless before consciousness gradually cleared. A few new blisters formed adjacent to the old ones before they all broke down, leaving encrusted, red-rimmed ulcers.

His treatment was symptomatic. Ample amounts of fluids were accepted orally when intake was encouraged. Mouth care was administered. Medication with aspirin and sponging with alcohol were used while the patient was febrile. Chloramphenicol (Chloromycetin) was administered for two days, and penicillin was given for three weeks (after a six-day interval) to combat skin infection.

As early as the second day of admission he was able to walk to the bathroom with help, and on the third day normal motor function had returned. The natural course of the intoxication, if the time of ingestion was correctly given, was five to six days. When the intoxication cleared, the returning symptoms of his primary disease required treatment with chlorpromazine, 300 mg. thrice daily, and trihexyphenidyl was resumed in doses of 2 mg. thrice daily because of the side effects of parkinsonism. The only residual signs of the intoxication were the skin ulcers, which took several weeks to heal. The patient was amnesic throughout the five days of this condition, his amnesia beginning shortly after the ingestion of the drug.

DISCUSSION

Most of these symptoms closely paralleled the well-known effects of intoxication with atropine. Cholinergic blockade was evident, and a toxic psychosis appeared with mixed central nervous

*From the Verdun Protestant Hospital, 6875 LaSalle Blvd., Verdun, Quebec.

Canad. Med. Ass. J.
July 14, 1962, vol. 87

system excitation and depression. The fever was probably due to suppression of sweating; this assumption is supported by the fact that hyperthermia is produced by atropine only in those animals whose thermoregulatory mechanisms include the secretion of sweat.[1] The pathogenesis of the skin lesions was obscure, but their distribution suggested that friction might have played a role.

This intoxication with massive overdosage is to be distinguished from those reactions due to idiosyncrasy to ordinary amounts of trihexyphenidyl; this idiosyncracy makes it impossible for 5 to 10% of patients to tolerate effective doses of this drug because of anhydrosis, xerostomia, stomatalgia, vertigo, agitation, disorientation, confusion and mild delirium.[2]

In addition to the treatment applied in this case, gastric lavage is recommended when the diagnosis is recognized in time, and stimulants or sedatives may be required for dangerous levels of depression or excitement, respectively. Pilocarpine or methacholine has been given to restore salivary flow; miotic agents are necessary in some cases to combat excessive mydriasis and cycloplegia. Darkening the room often relieves the discomfort due to photophobia.

SUMMARY

A case has been presented in which it was demonstrated that trihexyphenidyl (Artane) in massive overdosage may cause intoxication very similar to that caused by atropine, and may be treated in the same fashion.

REFERENCES

1. GOODMAN, L. S. AND GILMAN, A.: The pharmacological basis of therapeutics, 2nd ed., The Macmillan Company, New York, 1955, p. 551.
2. *Idem*: *Ibid.*, p. 210.

SHORT COMMUNICATION

Ventilatory Function in Normal Children

REUBEN M. CHERNIACK, M.D., F.R.C.P.[C], F.A.C.P., *Winnipeg, Man.*

AN assessment of ventilatory function is an integral part of the investigation of children with respiratory disease. In order to interpret such an assessment, however, it is essential to establish normal values for these measurements for children of the same age and body size. Although there are a number of reports of ventilatory measurements in normal children,[1-6] most deal with small numbers of subjects, and none assess the maximal mid-expiratory flow rate, which is a sensitive index of airway resistance. In addition, none of the measurements reported have been ascertained on children under 6 years of age.

This paper presents the normal values of ventilatory function obtained from 260 male and 261 female children whose ages varied from 3 to 17 years.

TABLE I.—FREQUENCY DISTRIBUTION AND RANGE OF HEIGHT AND WEIGHT OF SUBJECTS STUDIED

Age (years)	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*
Males														
Number of subjects	10	14	17	26	32	18	14	31	35	15	20	10	15	3
Range of height (cm.)	75–105	95–113	102–118	100–130	105–145	102–145	120–140	125–165	125–148	138–170	140–168	163–175	128–180	155–168
Range of weight (lb.)	28– 45	33– 58	35– 60	30– 65	40– 83	43– 68	45– 89	57–143	57–110	78–143	51–145	82–148	68–150	112–142
Females														
Number of subjects	4	9	20	23	28	34	32	22	23	27	16	13	8	2
Range of height (cm.)	80– 95	88–120	93–115	108–130	115–130	102–139	120–148	123–150	130–163	125–163	143–165	143–168	150–165	153–160
Range of weight (lb.)	24– 31	31– 44	34– 49	38– 82	41– 80	42– 83	40– 94	51– 95	61–125	51–117	76–148	83–160	94–130	110–118

METHODS

The children had no clinical or radiological evidence of cardiorespiratory disease and were selected from the wards and outpatient department of the Children's Hospital of Winnipeg. The number of children in each age group and the range of heights and weights are presented in Table I.

Vital capacity, maximum breathing capacity and maximal mid-expiratory flow rate were determined with a nine-litre Warren E. Collins spirometer, from which all valves and the carbon dioxide

From the Departments of Medicine and Pediatrics, University of Manitoba, and the Winnipeg Children's Hospital, Winnipeg, Manitoba.